SERION ELISA *classic*

Coxiella burnetii Phase 1 IgA / IgG
Coxiella burnetii Phase 2 IgG / IgM

CE

Instructions - English

(Version V 131.14)

virion\serion

Updates	
Current version Nr.:	**V 131.14**
Previous version:	**V 131.13**
Update in section:	**General Update**

SERION ELISA *classic* Coxiella burnetii Phase 1 IgA / IgG Coxiella burnetii Phase 2 IgG / IgM

CONTENTS

SERION ELISA *classic* Coxiella burnetii Phase 1 IgA / IgG and Coxiella burnetii Phase 2 IgG / IgM

Enzyme-immunoassay for determination of human antibodies

for *in vitro* diagnostic use

SERION ELISA *classic* Coxiella burnetii Phase 1 IgA	Order Nr.:	ESR1311A
SERION ELISA *classic* Coxiella burnetii Phase 1 IgG	Order Nr.:	ESR1311G
SERION ELISA *classic* Coxiella burnetii Phase 2 IgG	Order Nr.:	ESR1312G
SERION ELISA *classic* Coxiella burnetii Phase 2 IgM	Order Nr.:	ESR1312M

1 INTENDED USE

SERION ELISA *classic* Coxiella burnetii tests are recommended for the detection of human antibodies in serum or plasma directed against *Coxiella burnetii* in Phase 1 or Phase 2. SERION ELISA *classic* Coxiella burnetii IgM is recommended for the detection of acute Q-fever, while SERION ELISA *classic* Coxiella burnetii (Phase 2) IgG supports the differential diagnosis of infections of the respiratory tract, especially atypical pneumonia. SERION ELISA *classic* Coxiella burnetii (Phase I) tests are recommended for the diagnosis of chronic Q-fever. All SERION ELISA *classic* Coxiella burnetii are used for the serological therapy follow-up in acute and chronic diseases.

2 DIAGNOSTIC RELEVANCE

Coxiella burnetii is a gram-negative, aerobic coccobacillus of the *Coxiellaceae* family. The causative agent of the so called Q fever is extremely infectious and very resistant to environmental factors. Just a few bacteria can result in transmission and disease.

Q fever (Query Fever, Queensland Fever, Balkan Fever) was first described in 1937 by Edward Holbrook Derrick as an illness of unknown origin found in abattoir workers in Brisbane (Queensland, Australia). In the same year the causative agent was isolated by Frank Macfarlane Burnet and Mavis Freeman. Herald Rea Cox and Gordon Davis isolated the bacterium in 1938 from ticks in Nine Mile (Montana, USA) and described the transmission route. Finally, the pathogen was officially named as *Coxiella burnetii*.

Coxiella burnetii is – with the exception of New Zealand and Antarctica – distributed worldwide. Infected sheep are the primary source of infection for humans, however, household pets such as dogs or cats, as well as cattle and goats may also transmit the organism to humans.

Infection of humans may be caused by inhalation of infected dust, contact with contaminated wool, ingestion of animal products such as meat and milk or dairy products. In particular, contact with the afterbirth of infected farm animals is an important source of infection. Conversely, the transmission of pathogen from person to person has been described only in rare cases.

Approximately half of infected individuals exhibit no clinical symptoms. The most common manifestation following an incubation period of two to three weeks, are mild flulike symptoms with abrupt onset of fever, malaise, severe headache, myalgia, loss of appetite, dry cough, chest pain and chill, more seldom accompanied by gastrointestinal symptoms such as nausea, vomiting and diarrhea. During its course, the disease can progress to an atypical pneumonia, which may result in a life-threatening acute respiratory distress syndrome (ARDS). More seldom, Q fever presents as granulomatous hepatitis with inflammation of the liver. In rare cases, the disease takes a chronic course and presents as an inflammation of the inner lining of the heart muscle (endocarditis) or of the heart sac (pericarditis), which is usually fatal if untreated. However, with appropriate antibiotic treatment, the mortality rate falls to around 10 %.

The diagnosis of Q fever is performed by the demonstration of specific antibodies directed against *Coxiella burnetii*. Due to variations in the lipopolysaccharide (LPS) structure on the surface of the pathogen, as the disease enters the chronic state, and the subsequent associated immune response, a serological differentiation of acute from chronic infections is possible. Due to the high sensitivity and specificity necessary when performing a differential analysis of the antibody class-specific immune response directed against phase 1 and phase 2 antigens, the use of ELISA immunoassays is recommended by the World Health Organization (WHO). Following the regular course of an acute primary infection, specific IgM and IgG antibodies directed against the immunogenic phase 2 antigens can be demonstrated. IgG antibodies directed against phase 2 antigens often persist over several years. In the lead-up to a chronic infection, IgG and IgA antibodies directed against the phase 1 antigens appear, which are of diagnostic value particularly for the diagnosis of Q fever endocarditis.

3 TEST PRINCIPLE SERION ELISA *classic*

The ELISA (Enzyme Linked Immunosorbent Assay) is an immunoassay, which is particularly suited to the determination of antibodies in the field of infectious serology. The reaction is based on the specific interaction of antibodies with their corresponding antigen. The test strips of the SERION ELISA *classic* microtiter plate are coated with specific antigens of the pathogen of interest. If antibodies in the patient´s serum sample are present, they bind to the fixed antigen. A secondary antibody, which has been conjugated with the enzyme alkaline phosphatase, detects and binds to the immune complex. The colourless substrate p-nitrophenylphosphate is then converted into the coloured product p-nitrophenol. The signal intensity of this reaction product is proportional to the concentration of the analyte in the sample and is measured photometrically.

4 KIT COMPONENTS

Test Components	Pieces / Volume	
	Phase 2 IgG	**Phase 1 IgA / IgG Phase 2 IgM**
Break apart microtiter test strips each with eight antigen coated single wells, (altogether 96) MTP, 1 frame. The coating material is inactivated.	12 pieces	12 pieces
Standard serum (ready-to-use) STD, Human serum in protein containing phosphate buffer; negative for anti-HIV Ab, HBs-Ag (Hepatitis B-Virus surface antigen) and anti-HCV Ab; preservative: < 0.1 % sodium azide; colouring: Amaranth O	2 x 2 ml	-
Cut-off serum (ready-to-use) C/O, Human serum in protein containing phosphate buffer; negative for anti-HIV Ab, HBs-Ag (Hepatitis B-Virus surface antigen) and anti-HCV Ab; preservative: < 0.1 % sodium azide; colouring: Chinaldin yellow	-	2 x 2 ml
Positive control serum (ready-to-use) POS, Human serum in protein containing phosphate buffer; negative for anti-HIV Ab, HBs-Ag (Hepatitis B-Virus surface antigen) and anti-HCV Ab; preservative: < 0.1 % sodium azide; colouring: Amaranth O	-	2 ml
Negative control serum (ready-to-use) NEG, Human serum in protein containing phosphate buffer; negative for anti-HIV Ab, HBs-Ag (Hepatitis B-Virus surface antigen) and anti-HCV Ab; preservative: < 0.1 % sodium azide; colouring: Lissamin Green V	2 ml	2 ml
Anti-human IgA, IgG or IgM conjugate (ready-to-use) APC, Anti-human IgA, IgG or IgM polyclonal antibody, conjugated to alkaline phosphatase, stabilised with protein stabilisation solution; preservative: < 0.1 % methylisothiazolone, < 0.1 % bromnitrodioxane	13 ml	13 ml
Washing solution concentrate (sufficient for 1000 ml) WASH, Sodium chloride solution with Tween 20 and 30 mM Tris/HCl, pH 7.4; preservative: < 0.1 % sodium azide	33.3 ml	33.3 ml
Dilution buffer (ready-to-use) DILB, Protein containing phosphate buffer with Tween 20; preservative: < 0.1 % sodium azide; colouring: 0.01 g/l Bromphenol blue	2 x 50 ml	2 x 50 ml
Stopping solution (ready-to-use) STOP, < 0.1 N sodium hydroxide, 40 mM EDTA	15 ml	15 ml
Substrate (ready-to-use) pNPP, Para-nitrophenylphosphate in solvent free buffer; preservative: < 0.1 % sodium azide	13 ml	13 ml
Quality control certificate with standard curve and evaluation table INFO, (quantification of antibodies in IU/ml or U/ml)	2 pages	-
Quality control certificate INFO	-	1 page

5 MATERIAL REQUIRED BUT NOT SUPPLIED

- Common laboratory equipment
- For the IgM detection: SERION Rf-Absorbent (Order Nr. Z200 (20 ml))
- Photometer for microtiter plates with filter, wavelength 405 nm, recommended reference wavelength 620 nm - 690 nm (e.g. 650 nm)
- Microtiter plate washer
- Incubator 37 °C
- Moist chamber
- Distilled water
- Click-Clips (Order Nr. VT120.1)
- Optional: SERION ELISA *control*

6 STORAGE AND STABILITY

Reagent	**Storage**	**Stability**
Microtiter strips (coated with antigen)	unopened after opening at 2 – 8 °C in closed aluminum bag with desiccant	see expiry date 6 months
Control sera / Standard sera	unopened after opening at 2 – 8 °C	see expiry date 6 months
Conjugate	unopened after opening at 2 – 8 °C	see expiry date 6 months
Dilution buffer	unopened after opening at 2 – 8 °C	see expiry date 6 months
Washing solution	unopened / after opening at 2 – 8 °C working dilution at 2 – 8 °C working dilution at room temperature	see expiry date 2 weeks 1 week
Substrate	unopened after opening at 2 – 8 °C	see expiry date 6 months
Stopping solution	unopened after opening at 2 – 8 °C	see expiry date 6 months

7 TEST PROCEDURE SERION ELISA *classic*

7.1 General information

Optimum results can only be achieved if the instructions are strictly followed. Only use SERION ELISA *classic* reagents when using SERION ELISA *classic* immunoassays. The components must not be exchanged for reagents of other manufacturers. Standard and control sera of SERION ELISA *classic* immunoassays are defined exclusively for the test kit to be used and must not be used in other lots. Washing solution, substrate and stop solution can be used for all SERION ELISA *classic* immunoassays irrespective of the lot and the test.

Each SERION ELISA *classic* test contains a ready-to-use sample dilution buffer. In some cases the use of special dilution buffers is necessary to guarantee consistent quality and reliable results. The dilution buffers can be used irrespective of the lots.

There are three different conjugate concentrations for each immunoglobulin class (IgA, IgG, IgM), indicated on the label as + (low), ++ (medium) and +++ (high). Conjugates with the same concentration and of the same immunoglobulin class are interchangeable and can be used for other SERION ELISA *classic* immunoassays irrespective of the lot and the test. Dilution or alteration of the reagents may result in a loss of sensitivity. Use aseptic techniques when removing aliquots from the reagent tubes to avoid contamination.

Reproducibility of test results is dependent on thorough mixing of the reagents. Agitate the flasks containing control sera before use and also all samples after dilution (e.g. by using a vortex mixer).

Be sure to pipette carefully and comply with the given incubation times and temperatures. Significant time differences between pipetting the first and last well of the microtiter plate when dispensing samples and control sera, conjugate or substrate can result in different pre-incubation times, which may influence the precision and reproducibility of the results. Avoid exposure of reagents to strong light during storage and incubation.

Adequate washing avoids test unspecificities. Therefore, the washing procedure should be carried out carefully. All of the flat bottom wells should be filled with equal volumes of washing buffer. At the end of the procedure ensure that the wells are free of all washing buffer in order to avoid uncontrolled dilution effects. Avoid foaming!

Reagents must be tightly closed after use to avoid evaporation and contamination. Take care not to mix-up the caps of the bottles and/or vials.

The SERION ELISA *classic* immunoassay is only valid if the lot-specific validation criteria on the quality control certificate are fulfilled.

7.2 Sample Preparation and Storage

Lipaemic, hemolytic or icteric samples (serum or plasma) should only be tested with caution. Obviously contaminated samples should not be tested. Serum or plasma (EDTA, citrate, heparin) collected according to standard laboratory methods are suitable samples. Samples must not be thermally inactivated.

7.2.1 Dilution of Samples

Before running the test, patient samples (V_1) must be diluted in dilution buffer (V_2) as follows:

SERION ELISA *classic* Coxiella burnetii Phase 2 IgG:

$V_1 + V_2 = 1+500$	add	10 µl	patient´s sample
	each to	1000 µl	dilution buffer (= 1+100)
		50 µl	of the first dilution
	each to	200 µl	dilution buffer (= 1+4)

SERION ELISA *classic* Coxiella burnetii Phase 1 IgA, IgG:

$V_1 + V_2 = 1+100$	add	10 µl	patient´s sample
	each to	1000 µl	dilution buffer

After dilution and before pipetting into the microtiter plate the samples must be mixed thoroughly to prepare a homogenous solution.

SERION ELISA *classic* Coxiella burnetii Phase 2 IgM

Interference with rheumatoid factors

Rheumatoid factors are autoantibodies mainly of the IgM class, which preferably bind to IgG immune complexes. The presence of non-specific IgM antibodies (rheumatoid factors) can lead to false-positive results in the IgM assay. Furthermore, the possibility exists, that weak-binding pathogen-specific IgM antibodies may be displaced by stronger-binding IgG antibodies leading to a false-negative IgM result. Therefore it is necessary to pretreat samples with rheumatoid factor-absorbens prior to IgM detection (SERION Rf-Absorbent, Order Nr.: Z200 (20 ml/100 tests)). Rf-absorption is performed by incubation of the patient's sample in Rf-dilution buffer for 15 minutes at room temperature or over night at 4 °C. The test procedure is described in a separate instruction manual.

Before running the test, rheumatoid factor-absorbent (V_1) must be diluted 1+4 in dilution buffer (V_2).

$V_1 + V_2 = V_3$ (1 + 4)	add	200 µl	Rf-absorbent
	each to	800 µl	dilution buffer

Patient's samples (V_4) must be diluted in this Rf-dilution buffer (V_3):

$V_4 + V_3$ = 1+100	add	10 µl	patient's sample
	each to	1000 µl	Rf-dilution buffer

After dilution and before pipetting into the microtiter plate the samples must be mixed thoroughly to prepare a homogenous solution.

7.2.2 Sample Storage

The patient's samples should not be stored for more than 7 days at 2 – 8 °C. Extended storage is possible at ≤ -20 °C. Avoid repeated freezing and thawing of samples. Diluted samples can be stored at 2 – 8 °C for one week.

7.3 Preparation of Kit Reagents

Bring all reagents to room temperature before testing.

7.3.1 Microtiter Test Strips

The microtiter test strips labeled with abreviations for pathogen and immunoglobulin class are packed with a desiccant in an aluminum bag. To open the aluminum bag of the microtiter plate please cut off the top of the marked side only, in order to guarantee proper resealing. Take unrequired cavities out of the frame and put them back into the aluminum bag. Close bag carefully to ensure airtight conditions. Do not use the strips if the aluminum bag is damaged or if the bag with remaining strips and desiccant was not properly resealed.

7.3.2 Control Sera / Standard Sera (ready-to-use)

Control and standard sera are ready-to-use and must not be diluted any further. For each test run - independent of the number of microtiter test strips to be used - control and standard sera must be included. Standard and cut off sera should be set up in duplicate. Do not treat control sera with Rf-absorbent.

7.3.3 Anti-human IgA, IgG or IgM AP-Conjugate (ready-to-use)

The required conjugate concentration (+, ++, +++) is indicated on the quality control certificate. Please refer also to the specification on the label. Avoid contamination.

7.3.4 Washing Solution (Concentrate)

Dilute washing buffer concentrate (V_1) 1:30 with aqua dest. to a final volume of V_2. Bottles used for the working dilution should be cleaned regularly. Discard cloudy solutions.

Example:

Buffer concentrate (V_1)	Final volume (V_2)
33.3 ml	1000 ml
1.0 ml	30 ml

7.3.5 Dilution Buffer for Samples (ready-to-use)

Discard cloudy solutions.

7.3.6 Substrate (ready-to-use)

Substrate in unopened bottle may have a slightly yellow coloring, which does not reduce the quality of the product! Avoid contamination.

7.3.7 Stopping Solution (ready-to-use)

7.4 Overview - Test Procedure

SERION ELISA *classic*
Coxiella burnetii Phase 1 IgA/IgG
resp. Coxiella burnetii Phase 2 IgM qualitative
resp. Coxiella burnetii Phase 2 IgG quantitative

In case of IgM detection absorption of rheumatoid factor, see No. 7.2.1;
Incubation 15 minutes at room temperature or over night at 4°C

sample dilution[1]
(patient´s samples)
Phase 1 IgA/IgG and Phase 2 IgM: 1+100
resp. Phase 2 IgG: 1+500

Pipette diluted samples and ready-to-use control /
standard sera into the microtest wells (100 µl)

⇩

INCUBATION 60 min./ 37 °C
moist chamber

⇩

WASH (4 x 300 µl DIL WASH)[2]

⇩

Pipette conjugate solution APC (100 µl)

⇩

INCUBATION 30 min./ 37 °C
moist chamber

⇩

WASH (4 x 300 µl DIL WASH)[2]

⇩

Pipette substrate solution pNPP (100 µl)

⇩

INCUBATION 30 min./ 37 °C
moist chamber / dark incubation

⇩

Pipette stopping solution STOP (100 µl)

⇩

READ EXTINCTION at 405 nm

[1]Special dilution buffers for the following SERION ELISA *classic* tests:
Borrelia burgdorferi IgG, IgM and EBV EA IgG.

[2]For manual use:
tap plate at the end of the wash procedure on paper towel.

7.5 Manual Test Procedure

1. Place the required number of **cavities in the frame** and prepare a protocol sheet.
2. Add each **100 µl of diluted sample or ready-to-use controls** into the appropriate wells of microtiter test strips. Spare one well for substrate blank, e.g.:

Well	Quantitative ELISA	Qualitative ELISA
A1	substrate blank	substrate bank
B1	negative control	negative control
C1	standard serum	cut-off serum
D1	standard serum	cut-off serum
E1	patient 1 ...	positive control
F1	patient 2 ...	patient 1 ...

3. **Sample incubation** for 60 minutes (+/- 5 min.) at 37 °C (+/- 1°C) in moist chamber
4. After incubation **wash** all wells with washing solution (by automated washer or manually):
   - aspirate or shake out the incubation solution
   - fill each well with 300 µl washing solution
   - aspirate or shake out the washing buffer
   - repeat the washing procedure 3 times (altogether 4 times!)
   - dry by tapping the microtiter plate on a paper towel
5. **Addition of conjugate**
   Add 100 µl of the ready-to-use conjugate to the appropriate wells (except substrate blank)
6. **Conjugate incubation** for 30 minutes (+/- 1 min.) at 37 °C (+/- 1 °C) in moist chamber.
7. After incubation **wash** all wells with washing solution (see above).
8. **Addition of substrate**
   Add 100 µl of ready-to-use substrate solution to each well (including well for substrate blank!)
9. **Substrate incubation** for 30 minutes (+/- 1 min.) at 37 °C (+/- 1 °C) in moist chamber. Ensure dark incubation.
10. **Stopping of the reaction**
    Add 100 µl stopping solution to each well, shake microtiter plate gently to mix.
11. **Read extinction**
    Read optical desity (OD) within 60 minutes at 405 nm against substrate blank, reference wave length between 620 nm and 690 nm (e.g. 650 nm).

7.6 Automated Test Procedure

SERION ELISA are validated for use with Immunomat (using the following consumables: VT124, VT111, VT112) and suited for processing on similar analyzers. For processing on the Immunomat the current software version including reagent check has to be used. The automated processing is performed analogous to manual use. Please note, that under special working-conditions internal laboratory adaptations of the substrate incubation times may be necessary.

7.7 SERION ELISA *controls* (external Positive Control / Accuracy Control)

For the periodic verification of the test method, in order to fulfil the requirements of laboratory internal quality management systems, we recommend using SERION ELISA *controls* to determine precision and accuracy of SERION ELISA *classic* test runs. SERION ELISA *controls* are separately available and the usage is described in specific instruction manuals. SERION ELISA *controls* are not available in all countries and the customer should consult the local distributor.

8 TEST EVALUATION

8.1 SERION ELISA *classic* Coxiella burnetii Phase 1 IgA / IgG Coxiella burnetii Phase 2 IgG / IgM

The mathematical curve fitting for antibody quantification with SERION ELISA *classic* immunoassays is based on the 4-parameter logistic (4 PL) function.

$$Activity\ (U/ml) = e^{C-\frac{1}{B}\ln(\frac{D-A}{OD(Patient)*F-A}-1)}$$

The 4 parameters A, B, C, and D are representative for the exact shape of the standard curve:

Parameter A:	Lower asymptote (OD)
Parameter B:	Slope of the curve
Parameter C:	Inflection point
Parameter D:	Upper asymptote (OD)

Institut Virion\Serion GmbH establishes a lot-specific 4 PL standard curve for each SERION ELISA *classic* immunoassay in multiple test runs under optimal test conditions. The four parameters are indicated on the quality control certificate of each individual SERION ELISA *classic* test.

For the adaption of the test level to the given 4 PL standard curve the correction factor F is calculated by dividing the standard reference OD value indicated on the quality control certificate with the measured, and consequently test run-specific, standard OD value.

$$F = \frac{STD\ reference\ OD\ value}{measured\ STD\ OD\ value}$$

By multiplying the OD values obtained from patient samples with the correction factor F, the level of each individual test run is adjusted to the given 4 PL standard curve. Thereby, interassay deviations are compensated for and antibody activities can be directly evaluated from the 4 PL standard curve.

After subtraction of the substrate blank from all measured OD values and calculation of the mean OD value of the standard serum (STD), tested in duplicate, the evaluation of antibody activities from the optical measurement signals (OD) of patient samples can be performed with the 4PL function presented above.

8.2 Automated Evaluation / Software

For the automated evaluation of optical measurement signals, the Software SERION easy*ANALYZE* as well as the Microsoft® Excel®-based software tool SERION *activity* are available on request.

8.3 Borderline Range

The borderline range of the SERION ELISA *classic* Coxiella burnetii Phase 1 IgA / IgG Coxiella burnetii Phase 2 IgG / IgM test is specified on the quality control certificate and indicates the range of borderline test results. Values below this range indicate a negative test result; values above the borderline range are interpreted positive.

8.4 Limits of Quantification

The limits of quantification are specified on the quality control certificate of the SERION ELISA *classic* Coxiella burnetii Phase 1 IgA / IgG Coxiella burnetii Phase 2 IgG / IgM . The linearity of dilution within this range has been demonstrated in comprehensive evaluation studies. In case a patient sample shows a test result above the upper limit of quantification, the sample may be tested at a higher dilution. The resulting antibody activity must then be multiplied by the additional dilution factor.

8.5 Qualitative Evaluation with SERION ELISA *classic* Coxiella burnetii Phase 2 IgG

For the SERION ELISA *classic* test evaluation a lot-specific quality control certificate with standard curve and an evaluation table is included in the test kit so that the obtained OD values may be assigned to the corresponding antibody activities. The substrate blank must be subtracted from all OD values prior to evaluation. Mean OD value of the standard serum (STD), tested in duplicate, has to be used.

Method 1:
In the first line of the table, several ranges of OD values for the standard serum are depicted covering the whole standard validity range. According to the measured mean OD value of the standard serum, the corresponding column can be chosen. This column contains the information of upper and lower cut-off OD values to allow evaluation of the patient sample. OD values below the lower cut-off are evaluated negative and values above the upper cut-off are evaluated positive. Implementation of the correction factor F is not necessary in the context of the evaluation table.

Method 2:
Qualitative Evaluation

To fix the cut-off ranges multiply the mean value of the measured standard OD with the numerical data of the quality control certificate (see special case formulas), e.g.:

OD = 0.502 x MW(STD) with upper cut-off

OD = 0.352 x MW(STD) with lower cut-off

If the measured mean absorbance value of the standard serum is 0.64 OD, the range of the cut-off is in between 0.225-0.321 OD.

Calculation example:
Standard serum mean OD = 0.64
Upper cut-off: OD = 0.502 x 0.64 = 0.321
Lower cut-off: OD = 0.352 x 0.64 = 0.225

8.6 SERION ELISA *classic* Coxiella burnetii Phase 1 IgA / IgG Coxiella burnetii Phase 2 IgM

For the evaluation of test runs a lot-specific quality control certificate with declarations concerning cut off serum and positive control is included in every SERION ELISA *classic.*

Before evaluation the blank value (blank) has to be substracted from each sample value. For determination of the cut-off range in OD the mean of the readings for the cut-off serum has to be calculated. The cut-off range in OD corresponds to the mean value of the cut-off serum +/- 10 %.

OD sample	more than	10 % over	OD cut-off	positive
OD sample	+/-	10 % of	OD cut-off	borderline
OD sample	more than	10 % under	OD cut-off	negative

8.7 Criteria of Validity

The substrate blank must be < 0.25 OD.

The negative control must be negative.

By use of quantitative SERION ELISA *classic* tests the mean OD value (after subtraction of the substrate blank!) of the standard serum must be within the validity range, which is given on the lot specific quality control certificate.

By use of qualitative SERION ELISA *classic* tests the OD-value of the positive control and the mean OD value of the cut off serum must be within the validity ranges, which are given on the lot specific quality control certificate of the kit (after subtraction of the substrate blank!). This criterion is not applicable for qualitative evaluation of quantitative SERION ELISA *classic* tests.

The variation of OD values of the standard serum or cut off serum must not be higher than 20 %.

If these criteria are not met, the test is not valid and must be repeated.

8.8 Interpretation of Results

A positive test result confirms the presence of specific antibodies. A negative result indicates that no clinically relevant antibodies against the pathogen are present in the patient´s sample, but does not exclude the possibility of an acute infection. In case of a borderline result a reliable evaluation is not possible. A definitive diagnosis can only be achieved by testing paired serum samples, taken at one to two weeks intervals, in parallel.

The most important parameter for early detection of acute Q-fever infections is anti-phase 2 IgM. In the further progression of the acute course also phase 2 IgG antibodies appear.

The most important parameter for the detection of a chronic Q-fever infection is anti-phase 1 IgG. High anti-phase 2 IgG antibody titers with a simultaneous increase of anti-phase 1 antibody titers are diagnostically significant and show the beginning of a or *already existing chronic infection.*

Particularly in the case of Q-fever endocarditis, extremely high titers against antigens of phase 1 and 2 may occur. High IgA-levels against phase 1 antigens are significant and diagnostically meaningful in cases of endocarditis.

In cases of granulomatous hepatitis, only moderately high titers against phase 1 antigen with, very high titers against phase 2 antigen are observed. These patient´s sera usually show anti complementary activity. This is not the case with sera from endocarditis patients. The anti-phase 1 IgM-response is usually weak. Patients with chronic Q-fever are, in addition, strongly rheumatoid factor positive.

In the following table a summary of the characteristic reaction patterns of diverse clinical manifestations is given:

Antibody activity during an acute and chronic Q-fever disease:

	Phase 2		Phase 1	
	IgG	IgM	IgG	IgA
acute disease	++	+/++	(+)	-
chronic disease:				
granulomatous hepatitis	+++	++/+++	+/++	-/+
endocarditis	++/+++	+/++	++/+++	++/+++

Cross-reactions of antibodies directed against *Bartonella spp*., *Bordetella spp*., *Brucella spp*., *Legionella spp*. and *Mycoplasma pneumoniae* cannot be excluded.

8.9 Reference Range of Healthy Individuals

Testing of random blood donor sera, collected in the region of southern Germany, with SERION ELISA *classic* Coxiella burnetii Phase 1 IgA / IgG Coxiella burnetii Phase 2 IgG / IgM resulted in the following distribution:

SERION ELISA *classic*	Number	negative	borderline	positive
Coxiella burnetii Phase 2 IgG	105	104 (99.0 %)	-	1 (1.0 %)
Coxiella burnetii Phase 2 IgM	105	104 (99.0 %)	1 (1.0 %)	-
Coxiella burnetii Phase 1 IgA	105	100 (95.2 %)	1 (1.0 %)	4 (3.8 %)
Coxiella burnetii Phase 1 IgG	105	104 (99.0 %)		1 (1.0 %)

9 PERFORMANCE CHARACTERISTICS

9.1 Sensitivity and Specificity

The performance characteristics of the SERION ELISA *classic* Coxiella burnetii Phase 2 IgG test was determined with 77 sera from blood donors and from patients with suspected Q fever.

For the SERION ELISA *classic* Coxiella burnetii Phase 2 IgM test 273 sera from blood donors and patients with suspected Q fever infection were tested against a commercially available test.

The performance characteristics of the SERION ELISA *classic* Coxiella burnetii Phase 1 IgA and IgG test were evaluated with 54 serum samples from patients with suspected Q fever infection and 105 sera from blood donors in comparison to the complement fixation test (CFT). Since the CFT does not allow for the detection of IgA antibodies, the evaluation was performed with the assumption that the generation of IgA antibodies occurs in parallel with the formation of complement binding antibodies following the course of an infection.

	Sensitivity	Specificity
SERION ELISA *classic* Coxiella burnetii Phase 2 IgG	92.5 %	>99 %
SERION ELISA *classic* Coxiella burnetii Phase 2 IgM	94.4 %	>99 %
SERION ELISA *classic* Coxiella burnetii Phase 1 IgA / IgG	94.2 %	96.2 %

9.2 Reproducibility

SERION ELISA *classic* Coxiella burnetii Phase 1 IgA:

Sample	Mean Value (OD)	Intraassay CV (%)	Mean Value (OD)	Interassay CV (%)
Serum 1	0.153	6.0	0.156	16.3
Serum 2	0.814	6.8	0.721	9.1
Serum 3	1.696	4.1	1.512	6.3

SERION ELISA *classic* Coxiella burnetii Phase 1 IgG:

Sample	Mean Value (OD)	Intraassay CV (%)	Mean Value (OD)	Interassay CV (%)
Serum 1	0.188	3.2	0.207	13.0
Serum 2	0.363	2.6	0.366	8.2
Serum 3	0.788	3.1	0.852	4.5

SERION ELISA *classic* Coxiella burnetii Phase 2 IgG:

Sample	Mean Value (OD)	Intraassay CV (%)	Mean Value (OD)	Interassay CV (%)
Serum 1	0.116	3.6	0.127	12.2
Serum 2	1.490	2.5	1.552	6.3
Serum 3	1.865	3.0	1.912	7.0

SERION ELISA *classic* Coxiella burnetii Phase 2 IgM:

Sample	Mean Value (OD)	Intraassay CV (%)	Mean Value (OD)	Interassay CV (%)
Serum 1	0.060	6.2	0.087	10.4
Serum 2	1.529	2.7	1.632	4.5
Serum 3	1.695	1.7	1.773	5.0

9.3 Cross-reactivities

SERION ELISA *classic* Coxiella burnetii Phase 1 IgA
To determine detection of cross-reactive antibodies directed against different parameters sera were analyzed with SERION ELISA *classic* Coxiella burnetii Phase 1 IgA. Positive sera (10 sera each) for Brucella IgA, Mycoplasma pneumoniae IgA and Chlamydia IgG have been tested as well as sera positive for rheumatoid factor (RF) and anti-nuclear antibodies (ANA). Within this internal evaluation potential cross-reactivities with five Brucella IgA and three ANA positive serum samples have been observed. Other cross-reactivities cannot be ruled out in general.

SERION ELISA *classic* Coxiella burnetii Phase 1 IgG
To determine detection of cross-reactive antibodies directed against different parameters sera were analyzed with SERION ELISA *classic* Coxiella burnetii Phase 1 IgG and a commercially available anti- Coxiella burnetii Phase 1 IgG ELISA. Positive sera (10 sera each) for Brucella IgG, Mycoplasma pneumoniae IgG, Legionella pneumophila 1-7 IgG and Chlamydia IgG have been tested as well as sera positive for rheumatoid factor (RF) and anti-nuclear antibodies (ANA). Within this internal evaluation potential cross-reactivities with two Brucella positive serum samples have been observed. All reactivities have been confirmed by positive or borderline results in the reference assay. Other cross-reactivities cannot be ruled out in general.

SERION ELISA *classic* Coxiella burnetii Phase 2 IgG
To determine detection of cross-reactive antibodies directed against different parameters sera were analyzed with SERION ELISA *classic* Coxiella burnetii Phase 2 IgG and a commercially available anti- Coxiella burnetii Phase 2 IgG ELISA. Positive sera (10 sera each) for Brucella IgG, Mycoplasma pneumoniae IgG, Legionella pneumophila 1-7 IgG and Chlamydia IgG have been tested as well as sera positive for rheumatoid factor (RF)

and anti-nuclear antibodies (ANA). Within this internal evaluation potential cross-reactivities with one Legionella pneumophila 1-7 IgG and two Brucella IgG positive serum samples have been observed. All reactivities have been confirmed by positive or borderline results in the reference assay. Other cross-reactivities cannot be ruled out in general.

SERION ELISA *classic* Coxiella burnetii Phase 2 IgM
To determine detection of cross-reactive antibodies directed against different parameters sera were analyzed with SERION ELISA *classic* Coxiella burnetii Phase 2 IgM and a commercially available anti- Coxiella burnetii Phase 2 IgM ELISA. Positive sera (10 sera each) for Brucella IgM, Mycoplasma pneumoniae IgM, Legionella pneumophila 1-7 IgM and Chlamydia IgM have been tested as well as sera positive for rheumatoid factor (RF) and anti-nuclear antibodies (ANA). Within this internal evaluation potential cross-reactivities with one Brucella IgM and one Legionella pneumophila 1-7 IgM positive serum samples have been observed. All reactivities have been confirmed by positive or borderline results in the reference assay. Other cross-reactivities cannot be ruled out in general.

9.4 Interfering substances

SERION ELISA *classic* Coxiella burnetii Phase 1 IgA/IgG und Coxiella burnetii Phase 2 IgG/IgM
To determine the influence of interfering substances, sera with different reactivities were analyzed with SERION ELISA *classic* Coxiella burnetii Phase 1 IgA/IgG and Coxiella burnetii Phase 2 IgG/IgM. No interferences have been detected for sera with concentrations up to 2.00 g/L hemoglobin, 11.50 g/L lipemia/triglyceride or 0.201 g/L bilirubin (conjugated and unconjugated).

10 SAFETY MEASURES

10.1 Statements of Warning

The SERION ELISA *classic* is designed for use by qualified personnel who are familiar with good laboratory practice. All kit reagents and human specimens should be handled carefully, using established good laboratory practice.

- This kit contains human blood components. Although all control- and cut-off sera have been tested and found negative for anti-HIV-ab, HBs-Ag (*Hepatitis B-Virus-surface Antigen*) and anti-HCV-ab, they should be considered potentially infectious.
- Do not pipette by mouth.
- Do not smoke, eat or drink in areas in which specimens or kit reagents are handled.
- Wear disposable gloves, laboratory coat and safety glasses while handling kit reagents or specimens. Wash hands thoroughly afterwards.
- Patient’s material and other potentially infectious material should be decontaminated after the test run.
- Reagents should be stored safely and be inaccessible to unauthorized access e.g. children.

10.2 Disposal

Please observe the relevant statutory requirements!

10.3 Limitation of the test

Please note that diagnosis should never be solely based on serological data. Rather, serological results have to be interpreted in the context of the clinical picture and other diagnostic findings.

11 LITERATUR / REFERENCES / RÉFÉRENCES / BIBLIOGRAFIA / BIBLIOGRAFÍA / REFERÊNCIAS / ΑΝΑΦΟΡΕΣ / ODKAZY / BIBLIOGRAFIA / ЛИТЕРАТУРА / REFERENCER / REFERENSER / REFERENCIE / REFERENCE / REFERANSER / REFERENCIÁK

[1] Devine, P., Doyle, C., Lambkin, G. (1997) Combined determination of Coxiella burnetii-specific immunoglobulin M (IgM) and IgA improves specificity in the diagnosis of acute Q Fever. Clin. Diagn. Lab. Immunol. *4*, 384-6.

[2] Döller, G., Döller, P. C., Gerth, H.-J. (1984) Early diagnosis of Q-Fever: Detection of immunoglobulin M by radioimmunoassay and enzyme immunoassay. Eur. J. Clin. Microbiol. *3*, 550-3.

[3] Field, P. R., Hunt, J. G., Murphy, A. M. (1983) Detection and persistence of specific IgM antibody to Coxiella burnetii by enzyme-linked immunosorbent assay: a comparison with immunofluorescence and complement fixation tests. J. Infect. Dis. *148*, 477-87.

[4] Fournier, P.-E., Marrie, T. J., Raoult, D. (1998) Diagnosis of Q-Fever. J. Clin. Microbiol. *36*, 1823-34.

[5] Maurin, M., Raoult, D. (1999) Q Fever. Clin. Microbiol. Rev. *12*, 518-53.

[6] Musso, D., Raoult, D. (1997) Serological cross-reactions between Coxiella burnetii and Legionella micdadei. Clin. Diagn. Lab. Immunol. *4*, 208-12

[7] Peacock, M. G., Philip, R. N., Williams, J. C., Faulkner, R. S. (1983) Serological evaluation of Q Fever in humans: enhanced phase I titers of immunoglobulins G and A are diagnostic for Q Fever endocarditis. Infect. Immun. *41*, 1089-98.

[8] Peter, O., Dupuis, G., Peacock M. G., Burgdorfer, W. (1987) Comparison of enzyme-linked immunosorbent assay and complement fixation and indirect fluorescent-antibody tests for detection of Coxiella burnetii antibody. J. Clin. Microbiol. *25*, 1063-7.

[9] Peter, O., Dupuis, G., Bee, D., Luthy, R., Nicolet, J., Burgdorfer, W. (1988) Enzyme-linked immunosorbent assay for diagnosis of chronic Q Fever. J. Clin. Microbiol. *26*, 1978-82.

[10] Raoult, D. (1994) Diagnosis and treatment of chronic Q-Fever. LabMedica International, Sept.-Oct., 18-21.

[11] Robert Koch Institut (1999) Q-Fieber: Situation in Deutschland und Übersicht. Epidemiologisches Bulletin *33*, 245-7.

[12] Sawyer, L. A., Fishbein, D. B., McDade, J. E. (1987) Q Fever: Current concepts. Rev. Infect. Dis. *9*, 935-46.

[13] Schneider, T. *et. al*. (1993) Q-Fieber-Epidemie in Berlin. Dtsch. med. Wschr. *118*, 689-95.

[14] Schmeer, N., Krauss, H., und Schiefer, H. G. (1987) Q-Fieber. Dtsch. med. Wschr. *112*, 184-8.

[15] Schmeer, N., Krauss, H., Werth, D., Schiefer, H. G. (1987) Serodiagnosis of Q Fever by enzyme-linked immunosorbent assay (ELISA). Zbl. Bakt. Hyg. A *267*, 57-63.

[16] Waag, D., Chulay, J., Marrie, T., England, M., Williams, J. (1995) Validation of an enzyme immunoassay for serodiagnosis of acute Q Fever. Eur. J. Clin. Microbiol. Infect. Dis. *14*, 421-7.

[17] Worswick, D., Marmion, B. P. (1985) Antibody responses in acute and chronic Q Fever and in subjects vaccinated against Q Fever. J. Med. Microbiol. *19*, 281-96.

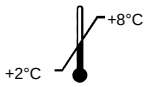
Symbole auf den Etiketten/ symbols on labels/ symboles et étiquettes/ simboli sulle etichette/ символы на этикетках/símbolos sobre las etiquetas/ σύμβολα στις ετικέτες/ símbolos nos rótulos / Symboly na štítcích / symboler på etiketter/ symboler på etiketterna/ Symbole na etykietach/ symboly na označení/ Simboli na oznakah/ symbol på etiketter

Hersteller/ Manufacturer/ Fabricant/ Produttore/Производитель/ Fabricante/ Κατασκευαστής/ Fabricante/ Výrobce/ Fremstiller/ Tillverkare/ Producent/ Výrobca/ Izdelovalec/ Produsent

Ausreichend für 96 Tests/ sufficient for 96 tests/ suffisant pour 96 tests/ sufficiente per 96 test/ достаточно для 96 тестов / suficiente para 96 pruebas/ επαρεκεί για 96 δοκιμασίες/ suficiente para 96 ensaios/ stačí na 96 testů/ nok til 96 test/ tillräckligt för 96 tester/ Wystarcza na 96 testów**/** postačuje na 96 testov/ Zadostuje za 96 testov/ Tilstrekkelig til 96 tester

LOT Charge/ lot/ lot / lotto/ lote/ παρτίδα/ lote/ šarže/ lot/ lot/ seria/ šarža/ serija/ lot /lot

REF Referenz oder Bestellnummer/ reference or order number/ numéro de référence ou de commande/ numero di riferimento o ordinazione/ ссылка или номер для заказа / referencia o número de pedido/ Αριθμός αναφοράς ή παραγγελίας/ referência ou número para encomenda/ reference nebo číslo objednávky/ reference eller bestillingsnummer/ referens eller beställningsnummer/ Numer referencyjny lub numer zamówienia/ referenčné číslo alebo číslo objednávky/ referenčna ali kataloška številka/ Referanse eller ordrenummer



Lagern zwischen 2 und 8 Grad Celsius/ store between 2 and 8 degree celsius/ entre 2 et 8 degré celsius/ conservare a temperatura compresa tra 2 e 8 gradi centigradi/ хранить при температуре от 2 до 8 градусов цельсия / conservar entre 2 y 8 grados celsius/ Φύλαξη μεταξύ 2 και 8 βαθμούς Κελσίου/ Armazenar entre 2º e 8º Celsius/ uchovávejte při teplotě 2 až 8 °C/ opbevares mellem 2 og 8 grader celsius/ förvara vid 2 till 8 grader Celsius/ Przechowywać w temp. pomiędzy 2 a 8 stopni Celsjusza/ skladovať pri teplote 2 až 8 stupňov Celzia/ Shranjujte pri temperaturi od 2 do 8 C/ Oppbevares mellom 2 og 8 grader Celsiu

CE CE-Markierung bei Erfüllung der IVD Richtlinie 98/79 EG/ CE marking according to IVD guideline 98/79 EC/ Étiquetage CE selon les directives DIV/ marcatura CE in conformità alla direttiva IVD 98/79 EC/ маркировка CE согласно директивам IVD 98/79 /marca CE según la directiva IVD 98/79 CE/ Σήμανση CE σύμφωνα με την οδηγία IVD 98/79 EE/ Marcação CE de acordo com a Directiva 98/79/ značení CE podle směrnice IVD 98/79/ES/ CE-mærkning iht. IVD-retningslinje 98/79/EF/ CE-märkning enligt riktlinjerna för IVD i direktiv 98/79/EC/ Oznakowanie CE zgodne z wytycznymi dot. diagnostyki in vitro 98/79 EC/ označenie CE podľa smernice IVD 98/79/ES/ oznaka CE, skladna s smernico IVD 98/79/ES/ CE-merking i henhold til IVD-retningslinjer 98/79/EØF

CE 0197 CE-Markierung bei Erfüllung der IVD Richtlinie 98/79 EG gemäß Anhang II, Liste B/ CE marking according to IVD guideline 98/79 EC according to annex II, list B/ Étiquetage CE selon les directives DIV 98/79 CE selon l'annexe II, liste B/ marcatura CE in conformità alla direttiva IVD 98/79 EC secondo l'allegato II, elenco B/ маркировка CE согласно директивам IVD 98/79, приложение II, список B / marca CE según la directiva IVD 98/79 CE de acuerdo con el anexo II, lista B/ Σήμανση CE σύμφωνα με την οδηγία IVD 98/79 EE, σύμφωνα με το παράρτημα II, κατάλογο B/ Marcação CE de acordo com a Directiva 98/79/ CE relativo aos dispositivos médicos de diagnóstico *in vitro*, segundo a lista B do anexo II/ značení CE podle směrnice IVD 98/79/ ES podle příloh II, seznamu B/ CE-mærkning iht. IVD-retningslinje 98/79 /EF iflg. anneks II, liste B/ CE-märkning enligt riktlinjerna för IVD i direktiv 98/79/EC, bilaga II, lista B/ Oznakowanie CE zgodne z wytycznymi dot. diagnostyki in vitro 98/79 EC, zgodnie z aneksem II, lista B/ označenie CE podľa smernice IVD 98/79 ES v znení dodatku II, zoznam B/ oznaka CE, skladna s smernico IVD 98/79/ES in seznamom B v Dodatku II/ CE-merking i henhold til IVD-retningslinjer 98/79/EØF, tillegg II, liste B

Verfallsdatum/ expiry date/ date d'expiration/ data di scadenza/ срок годности до /fecha de caducidad/ ημερομηνία λήξης/ data de validade/ datum exspirace/ udløbsdato/ förfallodatum/ data upływu ważności/ dátum exspirácie/ datum izteka roka uporabnosti/ utløpsdatp

MTP Mikrotiterplatte (brechbare Streifen)/ microtiter plate (breakable strips)/ plaque de microtitration (bandelettes détachables)/ piastra per microtitolazione (strisce separabili)/ микротитровальная панель (отрывные стрипы) /placa de microtitulación (tiras rompibles)/ Πλάκα μικροτιτλοποίησης (αποσπωμενες ταινίες)/ placa de microtitulação (tiras quebráveis)/ mikrotitrační deska (rozlomitelné proužky)/ mikrotiterplade (afbrækkelige strimler)/ mikrotiterplatta (brytbara strips)/ Płytka mikrotitracyjna (paski do odrywania)/ mikrotitračná platnička (rozlomiteľné prúžky)/ vsebnik za mikrotitriranje (z razdelki, ki jih je mogoče odlomiti)/ Mikrotiterplate (avbrytbare strips)

AG Antigen/ antigen/ Antigène/ antigene/ антиген /antígeno/ αντιγόνο/ antigénio/ antigen/ antigen/ Antygen/ antigén/ antigen/ Antigen

AK Antikörper/ antibodies/ Anticorps/ anticorpi/ антитела / anticuerpos/ αντίσωμα/ anticorpos/ protilátky/ antistoffer/ antikroppar/ Przeciwciała/ protilátky/ protitelesa/ Antistoffer

CAG Kontrollantigen/ control antigen/ antigène de contrôle/ antigene di controllo/ контрольный антиген /antígeno de control/ αντιγόνο ελέγχου/ antígeno de controre/ kontrolní antigen/ kontrolantigen/ kontrollantigen/ antygen kontrolny/ kontrolný antigén/ kontrolni antigen/ kontrollantigen

STD Standardserum/ standard serum/ Sérum standard/ siero standard/ стандартная сыворотка /suero patrón/ πρότυπος ορός/ soro padrão/ standardní sérum/ standardserum/ standardserum/ Surowica standardowa/ štandardné sérum/ standardni serum/ Standardserum

POS Positivkontrolle/ positive control/ Contrôle positif/ controllo positivo/ положительные контроли /control positivo/ θετικός έλεγχος/ controlo positivo/ pozitivní kontrola/ positiv kontrol/ positiv kontroll/ Kontrola pozytywna/ pozitívna kontrola/ pozitivna kontrola/ Positiv kontroll

C/O Grenzwertiges Serum/ cut-off serum/ Sérum seuil/ siero cut-off/ сомнительные сыворотки (пограничные)/suero de corte/ οριακός ορός (cut-off)/ soro *cut-off*/ cut-off sérum/ cutoff-serum/ cutoff-serum/ Surowica „cut-off"/ sérum na určenie hraničnej hodnoty/ mejni serum/ Stoppserum

NEG Negativkontrolle/ negative control/ Contrôle négatif/ controllo negativo/ отрицательные контроли /control negativo/ αρνητικός έλεγχος/ controlo negativo/ negativní kontrola/ negativ kontrol/ negativ kontroll/ Kontrola negatywna/ negatívna kontrola/ negativna kontrola/ Negativ kontroll

APC Alkalisches Phosphatase Konjugat antihuman/ alkaline phosphatase conjugate anti-human/ conjugué phosphatase alcaline anti-humain/ coniugato con fosfatasi alcalina anti-umano/ античеловеческий щелочной конъюгат фосфатазы / conjugado anti humano de fosfatasa alcalina/ Σύζευξη αλκαλικής φωσφατάσης/ conjugado anti-humano com fosfatase alcalina/ konjugát alkalické fosfatázy anti-humánní/ alkalisk phosphatase konjugat antihumant/ antihumant alkaliskt fosfatas-konjugat/ Anty-ludzki koniugat fosfatazy alkalicznej/ konjugát antihumánnej alkalickej fosfatázy/ konjugat alkalne fosfataze, antihumani/ Alkalisk fosfatase-konjugat, anti-humant

+ niedrig-konzentriertes Konjugat/ conjugate with low concentration/ conjugué à faible concentration/ coniugato a concentrazione bassa/ конъюгат низкой концентрации /conjugado con concentración baja/ Σύζευξη χαμηλής συγκέντωσης/ conjugado de baixa concentração/ konjugát s nízkou koncentrací/ konjugat med lav koncentration/ konjugat med låg koncentration/ koniugat o niskim stężeniu/ konjugát so strednou koncentráciou/ konjugat z majhno koncentracijo/ Konjugat med lav konsentrasjon

++ mittel-konzentriertes Konjugat/ conjugate with medium concentration/ conjugué à concentration moyenne/ coniugato a concentrazione media/ конъюгат средней концентрации /conjugado con concentración media/ Σύζευξη μέτριας συγκέντρωσης/ conjugado de concentração intermédia/ konjugát se střední koncentrací/ konjugat med medium koncentration/ konjugat med medelhög koncentration/ koniugat o średnim stężeniu/ konjugát so strednou koncentráciou/ konjugat s srednjo koncent/ Konjugat med middels konsentrasjon

+++ hoch-konzentriertes Konjugat/ conjugate with high concentration/ conjugué à concentration élevée/ coniugato a concentrazione alta/ высококонцентрированный конъюгат/ conjugado con concentración alta/ σύζευξη υψηλής συγκέντρωσης/ conjugado de elevada concentração/ konjugát s vysokou koncentrací/ konjugat med høj koncentration/ konjugat med hög koncentration/ koniugat o wysokim stężeniu/ konjugát s vysokou koncentráciou/ konjugat z veliko koncentracijo/ Konjugat med høy konsentrasjon

RF Rheumafaktor-Absorbens (Rf-Absorbens)/ rheumatoid factor absorbent (rf-absorbent)/ absorbant de facteur rhumatoïde (rf-absorbant)/ adsorbente del fattore reumatoide (adsorbente Rf)/ абсорбент ревматоидного фактора (Rf-абсорбент) /absorbente de factor reumatoide (material absorbente de Rf)/ Απορροφητής ρευματοειδούς παράγοντα (απορροφητής Rf)/ absorvente de factor reumatóide (absorvente de Fr)/ absorbent revmatoidního faktoru (rf-absorbent)/ reumafaktor-absorptionsmiddel (rf-absorptionsmiddel)/ reumafaktor-absorptionsmedel (rf-absorptionsmedel)/ Absorbent czynnika reumatoidalnego (absorbent RF)/ absorbent reumatoidného faktora (absorbent rf)/ absorbent revmatoidnega faktorja (absorbent RF)/ Revmatoid faktor-absorbent (rf-absorbent)

DILB
DILBS1
DILBS2 Verdünnungspuffer für Serum/ dilution buffer for sera/ sérum pour le tampon de dilution/ tampone di diluizione per sieri / разбавляющий буфер для сыворотки / solución amortiguadora para los sueros/ ρυθμιστικό διάλυμα αραίωσης για ορούς/ tampão de diluição para soro/ ředicí pufr pro séra/ fortyndingsbuffer til sera/ spädningsbuffert för serum/ bufor rozcieńczający do surowic / pufor na riedenie sér/ pufer za redčenje seruma/ Fortynningsbuffer til serum

WASH Waschlösungskonzentrat/ washing solution concentrate/ concentré de solution de lavage / soluzione di lavaggio concentrata / промывочный концентрат /concentrado de solución de lavado/ συμπύκνωμα έκπλυσης/ concentrado de solução de lavagem/ koncentrát promývacího roztoku/ vaskeopløsningskoncentrat/ tvättlösningskoncentrat/ Stężony roztwór do płukania/ koncentrát premývacieho roztoku/ koncentrat za raztopino za izpiranje/ Vaskeløsningskonsentrat

pNPP pNPP Substrat/ pNPP substrate/ substrat Pnpp/ substrato pNPP/ pNPP субстрат / sustrato pNPP/ Υπόστρωμα pNPP/ substrato pNPP/ pNPP substrát/ pNPP-substrat/ pNPP-substrat/ Substrat pNPP/ substrát pNPP/ substrat pNPP/ pNPP-substrat

STOP Stopplösung/ stopping solution/ solution d'arrêt/ soluzione di arresto/стоп-раствор/ solución de parada/ διάλυμα διακοπής/ solução de paragem/ zastavovací roztok/ stopopløsning/ stopplösning/ roztwór zatrzymujący reakcję/ ukončovací roztok/ raztopina za ustavitev reakcije/ stoppeløsning

INFO Gebrauchsanweisung, Zertifikat (Standardkurve und Auswertetabelle), CD/ instructions, certificate (standard curve and evaluation table), CD/ instructions, certificat (courbe de référence et tableau d'évaluation), CD/ istruzioni per l'uso, certificato (curva standard e tabella interpretativa), CD/ Инструкция по применению, сертификат (стандартная кривая и таблица для оценки), компактный диск /instrucciones, certificado (curva patrón y tabla de evaluación), CD/ Οδηγίες χρήσης, Πιστοποιητικό (πρότυπη καμπύλη και πίνακας υπολογισμού), CD/ instruções, certificado (curva padrão e tabela de avaliação), CD/ (standardní křivka a vyhodnocovací tabulka), CD/ brugsanvisning, certifikat (standardkurve og evalueringstabel), CD/ instruktioner, certifikat (standardkurva och utvärderingstabell), CD/ Instrukcje, certyfikat (krzywa standardowa i tabela do określania wyników/ CD/ pokyny, certifikát (štandardná krivka a hodnotiaca tabuľka), disk CD/ navodila, certifikat (standardna krivulja in ocenjevalna tabela), CD/ Instruksjoner, sertifikat (standardkurve og evalueringstabell), CD

RTU gebrauchsfertig/ ready-to-use/ prêt à l'emploi/ pronto per l'uso/ готовый к использованию /listo para usar/ έτοιμο προς χρήση/ pronto a utilizar/ připravený k použití/ klar til brug/ bruksfärdig/ gotowy do użycia/ pripravené na použitie/ pripravljen za uporabo/ klar til bruk

CONC Konzentrat/ concentrate/ concentré/ concentrato/ концентрат / concentrado/ Συμπύκνωμα/ concentrado/ koncentrát/ koncentrat/ koncentrat/ Koncentrat/ koncentrát/ koncentrat/ Konsentrat

DIL verdünnen oder lösen in/ dilute or disolve in/ diluez ou dissoudre dans/ diluire o sciogliere in/ разбавить или растворить в /diluir o disolver en/ αραίωση ή διάλυση σε/ diluir ou dissolver em/ nařeďte nebo rozpusťte v/ fortynd eller opløs i/ späd eller lös i/ Rozcieńczyć lub rozpuścić w/ rozriediť alebo rozpustiť v/ razredčite ali raztopite v/ Fortynnes eller løses opp i

AQUA destilliertes Wasser/ aqua detillata/ eau distillée/ acqua distillata/ дистиллированная вода /agua destilada/ αποσταγμένο νερό/ água destilada/ destilovaná voda/ destilleret vand/ destillerat vatten/ woda destylowana/ destilovaná voda/ destilirana voda/ Destillert vann

IVD In-vitro Diagnostik Anwendung/ in-vitro diagnostic use/ utilisation en diagnostic in-vitro/ uso diagnostico in vitro/ использование в диагностике ин-витро /uso diagnóstico in-vitro/ Διάγνωση, χρήση in-vitro/ para diagnóstico *in vitro*/ diagnostické použití in-vitro/ til in-vitro diagnostik/ *in vitro*-diagnostisk användning/ do diagnostyki in vitro/ diagnostické použitie in-vitro/ uporaba pri diagnostiki *in vitro*/ In vitro-diagnostisk bruk

Gebrauchsanweisung beachten/ consult instructions for use/ se référer à la notice d'instruction/ consultare le istruzioni per l'uso/ ознакомьтесь с инструкцией по использованию/ consúltense las instrucciones de uso/ συμβουλευτείτε τις οδηγίες χρήσης/ consultar as instruções de utilização/ čtěte návod k použití/ se brugsanvisningen/ se bruksanvisningen/ zapoznaj się z instrukcją stosowania/ dodržuj návod na použitie/ glejte navodila za uporabo/ se bruksanvisningen/ figyelembe kell venni a használati utasítást

SERION ELISA *classic*

102	Masern Virus / Measles Virus / Rougeole
103	Mumps Virus / Parotitis virus / Oreillons
104	Varicella-Zoster Virus (VZV)
105	Herpes simplex Virus 1/2
1051	Herpes simplex Virus 1
1052	Herpes simplex Virus 2
106	Legionella pneumophila 1-7
107	Echinococcus
108	Tetanus
109	Cytomegalovirus
110	Toxoplasma gondii
112	FSME Virus / TBE Virus
113	Resp. Syncytial Virus (RSV)
114	Dengue Virus/ Dengue
116	Brucella
117	Candida albicans
118	Helicobacter pylori
120	Bordetella pertussis
1201	Bordetella pertussis Toxin
121	Borrelia burgdorferi
122	Parvovirus B19
1231	Influenza A Virus
1232	Influenza B Virus
125	Leptospira
126	Parainfluenza Virus
127	Mycoplasma pneumoniae
128	Adenovirus
129	Röteln Virus / Rubella virus / virus de rubéole
130	Diphtherie / Diphtheria
1311	Coxiella burnetii (Q-Fieber) Phase 1 / Coxiella burnetii (Q-fever) phase 1
1312	Coxiella burnetii (Q-Fieber) Phase 2 / Coxiella
132	Aspergillus fumigatus
133	Enterovirus
134	Coxsackievirus
135	Echovirus
1361	Epstein-Barr Virus VCA
1362	Epstein-Barr Virus EBNA 1
1363	Epstein-Barr Virus Early Antigen
137	Chlamydia
1371	Chlamydia pneumoniae
1372	Chlamydia trachomatis
138	Yersinia
139	Campylobacter jejuni
141	West Nile Virus
142	Francisella tularensis
147	Leishmania

Manufacturer

Institut Virion\Serion GmbH
Friedrich-Bergius-Ring 19
97076 Würzburg, Germany

Tel. +49 (0) 931 3045 0 Fax +49 (0) 931 3045 100
Mail info@virion-serion.de
Web www.virion-serion.de

09/2018